UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte JEFFRY D. WATKINS and BARRETT ALLAN

Appeal 2007-2523
Application 10/370,749
Technology Center 1600

Decided: September 12, 2007

Before TONI R. SCHEINER, DONALD E. ADAMS, and
ERIC GRIMES, *Administrative Patent Judges.*

GRIMES, *Administrative Patent Judge.*

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a composition containing a polypeptide variant. The Examiner has rejected the claims as anticipated. We have jurisdiction under 35 U.S.C. § 6(b). We reverse.

BACKGROUND

The "'Fc region' refers to a C-terminal region of an immunoglobulin heavy chain" (Specification 36). "The Fc region . . . generally comprises

two constant domains" (*id.*) and is "involved in non-antigen binding functions" (*id.* at 1). For example, it "binds Fc receptors, which may trigger . . . antibody dependent cellular cytotoxicity (ADCC)" (*id.* at 2).

The Specification refers to "compositions comprising a variant . . . of a parent polypeptide having at least a portion of an Fc region, wherein the variant mediates antibody-dependent cell-mediated cytotoxicity (ADCC) in the presence of effector cells more effectively than the parent polypeptide and comprises at least one amino acid modification at position 280 in the Fc region" (*id.*). Specifically, the Specification describes an "amino acid modification at position 280 in the Fc region selected from D280H, D280Q, and D280Y"; i.e., substitution of histidine (H), glutamine (Q), or tyrosine (Y) for the naturally occurring aspartic acid (D) at position 280 (*id.* at 3). The Specification also describes a variant comprising an antibody or immunoadhesin (*id.* at 4).

DISCUSSION

1. CLAIMS

Claims 1-3, 5-8, and 10 are on appeal. Claims 11-20 are also pending but have been withdrawn from consideration by the Examiner. We will focus on claim 1, the broadest claim on appeal, which reads as follows:

> 1. A composition comprising a variant of a parent polypeptide having at least a portion of an Fc region, wherein said variant mediates antibody-dependent cell-mediated cytotoxicity (ADCC) in the presence of effector cells more effectively than said parent polypeptide, wherein said variant comprises a histidine, glutamine or tyrosine amino acid at position 280 in the Fc region, and wherein said parent polypeptide is an antibody or immunoadhesin.

2. PRIOR ART

The Examiner relies on the following reference:

Presta	US 6,737,056	May 18, 2004

3. ANTICIPATION

Claims 1-3, 5-8, and 10 stand rejected under 35 U.S.C. § 102(e) as anticipated by Presta. The Examiner finds that "Presta teaches . . . a polypeptide (e.g. antibody or immunoadhesin) comprising a variant Fc region with higher binding affinity to FcγR including FcγRIII and an amino acid substitution at positions such as 280 in the CH2 region for improved antibody-dependent cell-mediate[d] cytotoxicity" (Answer 4). The Examiner also finds that "Presta defines that the amino acid substitution refers to the replacement of [an] existing amino acid residue in a predetermined amino acid sequence with another different amino acid resid[u]e including histidine, glutamine, or tyrosine" (*id.*). In addition, the Examiner finds that "Presta teaches that the polypeptide comprising a variant Fc region can be formulated into [a] composition for diagnostic and therapeutic applications" (*id.*).

Appellants argue that Presta "neither expressly discloses nor clearly names histidine, glutamine, or tyrosine as species within the immense genus set forth as 'amino acid modifications' for position 280, nor does [Presta] ever expressly disclose or clearly name histidine, glutamine or tyrosine as members of the smallest identified preferred subgenus, 'amino acid substitution'" (Br. 10). Instead, Appellants argue that the "only species for modified amino acids at position 280 ever clearly named within [Presta] are D280A (alanine amino acid substituted for aspartic acid amino acid,

Table 6), D280N (asparagine substituted for aspartic acid, Table 8) and D280S (serine substituted for aspartic acid, Table 8)" (*id.*)

Specifically, Appellants argue that, "[e]ven though Column 12 of [Presta] lists the twenty amino acids known to be naturally occurring, the patent clearly states that 'amino acid substitution' includes *natural and non-natural* amino acids. Therefore, [Presta] identifies 'amino acid substitution' as the smallest preferred embodiment within the 'amino acid modification' genus, yet this subgenus is quite large indeed!" (Br. 11.) "Presta never states that natural amino acids are a preferred subgenus of this immense genus" (Reply Br. 2). Thus, Appellants argue, "the genus that was identified - - amino acid substitutions - - is too large for one of skill in the field to envisage *each member*" (Br. 11).

We reverse the rejection. Presta refers to "a variant of a parent polypeptide comprising an Fc region, which variant mediates antibody-dependent cell-mediated cytotoxicity (ADCC) in the presence of human effector cells more effectively or binds an Fc gamma receptor (FcγR) with better affinity, than the parent polypeptide and comprises at least one amino acid modification in the Fc region" (Presta, col. 4, ll. 30-36). Presta states that, "[b]y introducing the *appropriate* amino acid sequence modifications in a parent Fc region, one can generate a variant Fc region which (a) mediates antibody-dependent cell-mediated cytotoxicity (ADCC) in the presence of human effector cells more effectively and/or (b) binds an Fc gamma receptor (FcγR) with better affinity than the parent polypeptide" (*id.* at col. 21, ll. 60-66 (emphasis added)). Presta states that, "[g]enerally, the modification entails one or more amino acid substitutions" (*id.* at col. 19, ll. 47-48).

Presta also discloses that the "polypeptide variant may . . . comprise an antibody or an immunoadhesin" (*id.* at col. 4, ll. 36-37).

Presta defines an "amino acid modification" as "the substitution or deletion of the specified residue, or the insertion of at least one amino acid residue adjacent the specified residue" (*id.* at col. 12, ll. 26-30). In addition, Presta defines an "amino acid substitution" as "the replacement of at least one existing amino acid residue . . . with another different 'replacement' amino acid residue" (*id.* at col. 12, ll. 34-37). Presta states that the replacement residue may be a naturally occurring amino acid residue "(i.e. encoded by the genetic code)" selected from a list of the twenty standard amino acid residues or a non-naturally occurring amino acid residue (*id.* at col. 12, ll. 37-49).

As a variant with altered Fc gamma receptor binding affinity, Presta refers to a polypeptide comprising an amino acid modification at "one or more of" 66 amino acid positions of the Fc region, including position 280 (*id.* at col. 4, ll. 46-55). As a variant with improved Fc gamma receptor binding, Presta refers to a polypeptide comprising an amino acid modification at "one or more of" 32 amino acid positions of the Fc region, including position 280 (*id.* at col. 5, ll. 31-40). As a variant with increased FcγRII binding, Presta refers to a polypeptide comprising an amino acid modification at "one or more of" 28 amino acid positions of the Fc region, including position 280 (*id.* at col. 5, ll. 48-53). In addition, Presta identifies 16 amino acid positions, including position 280, as providing "improved binding to FcγRII and no effect on FcγRIII binding" (*id.* at Table 2). At the

280 position, Presta describes replacing the aspartic acid (D) with alanine (A), asparagine (N), or serine (S) (*id.* at Tables 6 and 8).

"Under 35 U.S.C. § 102, every limitation of a claim must identically appear in a single prior art reference for it to anticipate the claim." *Gechter v. Davidson*, 116 F.3d 1454, 1457 (Fed. Cir. 1997). In addition, a disclosure that allows one skilled in the art to "at once envisage each member of [a] limited class" describes each member of the class "as if [the reference] had drawn each structural formula or had written each name." *In re Petering*, 301 F.2d 676, 681-82 (CCPA 1962).

In this case, we agree with Appellants that the generic teaching in Presta of an amino acid substitution at one or more of various amino acid positions does not anticipate every polypeptide within this broad teaching. In particular, we agree with Appellants that one skilled in the art would not "at once envisage each member of" this broad class "as if [Presta] had drawn each structural formula or had written each name."

In rejecting the claims, the Examiner relies on Presta's definition of "amino acid substitution," which lists the twenty standard amino acids (Answer 6). However, this definition does not describe substituting the amino acid at position 280 with any of these twenty amino acids. Instead, unlike in *Ex parte A*, 17 USPQ2d 1716, 1718 (BPAI 1990), relied upon by the Examiner, it is necessary to select portions of the subject matter of claim 1 from various sections of Presta and combine them. As a result, we do not agree that Presta provides a specific teaching of substituting the amino acid at position 280 with each of these twenty amino acids and therefore with the three amino acids recited in claim 1. Thus, we agree with

Appellants that the Examiner has not set forth a prima facie case that Presta anticipates claims 1-3, 5-8, and 10.

SUMMARY

The Examiner has not shown that the claims were anticipated by the applied reference. We therefore reverse the rejection of claims 1-3, 5-8, and 10.

REVERSED

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ELI LILLY & COMPANY
PATENT DIVISION
P.O. BOX 6288
INDIANAPOLIS IN 46206-6288